Retention of Asbestos Fibers in the Human Body

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The number, type, and size of retained asbestos fibers were measured by scanning electron microscopy (SEM) in lung tissues of 10 workers who had died from lung cancer or mesothelioma. The levels were 190–3000 x 10^6 fibers/g of dry tissue in three crocidolite sprayers, 6–39 x 10^6 fibers/g of dry tissue in two asbestos product workers and 13–280 x 10^6 fibers/g of dry tissue in five insulators exposed to anthophyllite. The duration of past exposure corresponding to the limit of 1 million fibers/g of dry tissue was 1 to 2 days in spraying, 3 to 10 days at the production plant and 1 to 4 months in insulation work. No long-term clearance of amphibole fibers, >5 μm in length, could be demonstrated. In one of the sprayers the fiber concentrations of lung parenchyma, visceral and parietal pleura, hilar lymph nodes, and kidney cortex were orders of magnitude higher than in a series of unselected autopsies. The size and aspect ratio of crocidolite fibers in various tissues were similar, indicating that the translocation processes are rather unselective in respect to fiber dimensions. — Environ Health Perspect 102(Suppl. 5):253–255 (1994)

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Introduction

Inhaled and deposited particles are removed from the lungs by clearance mechanisms such as mucociliary transport, translocation to lymph nodes, migration, diffusion, and dissolution in body fluids. Because the long-term deposition and clearance rates of asbestos fibers cannot be directly measured in humans, data on the phenomena are derived from the analyses of retained particles in various tissues obtained during surgery or at autopsy of exposed workers. This requires that the past exposures of the subjects be known and not confounded by more recent events.

Even if asbestos dusts are polydisperse, their count median sizes are generally within a range where the probability of alveolar deposition is relatively uniform at approximately 10% (*1,2*). Short fibers are more easily removed from the lung, the clearance rate decreasing inversely with fiber length (*3–5*). Size distributions of retained fibers and dust samples from the Paakkila mine, Finland, indicate that anthophyllite fibers >5 to 17 μm in length or >0.6 μm in diameter persist permanently in the lungs. The retention data from anthophyllite, amosite and crocidolite miners have shown differences in fibrogenic potential that are the consequence of varying fiber size rather than the type of amphibole mineral (*3,6*). In a pathological series, including asbestosis, mesothelioma, and lung cancer, the size parameters of a specified amphibole have been similar irrespective of the disease category (*7,8*).

The main storage compartment of fibers in the human body appears to be the lung parenchyma, but high levels of asbestos fibers are also found in pleura, lymph nodes and kidney (*1,9–11*). The transport routes to extrapulmonary organs are not firmly established. Some studies in humans suggest that deposited fibers are translocated to parietal pleura and lymph nodes by direct, systemic, or lymphatic mechanisms. The accumulation of uncoated short fibers in lymph nodes has meant that they have the highest numerical concentrations that occur anywhere in the human body. The pathway to the kidneys probably depends on passive transport in the bloodstream as either bare or phagocytized particles (*1,4*).

Several hundreds of lung samples from mesothelioma, lung cancer, and asbestosis patients have been analyzed by electron microscopy at the Institute of Occupational Health, Helsinki (*12–14*). The selection criteria of known exposures were met for a series of cancer cases who had been heavily exposed to amphibole asbestos several decades ago. In these persons, the inhaled doses were quantifiable from the duration of employment, fiber concentrations in workplace air, and estimated volumetric rate of inhalation. Comparison of calculated doses with lung retention data yielded useful indices that related the individual work history in typical occupations to measured fiber levels in the lungs. In those calculations, the clearance of amphibole asbestos was assumed to be negligible, i.e., the effect of varying time from the exposure to the date of tissue sampling was not taken into account. In some cases the maximum feasible clearance rates can be calculated and expressed in terms of half-time estimates.

Materials and Methods

Three crocidolite sprayers, two asbestos product workers, and five insulators were selected as representative cases for long-term retention of asbestos fibers. The workers had been heavily exposed to crocidolite or anthophyllite asbestos, which was verified by lung dust analyses and personal interviews during hospitalization. The occupations, exposure times, levels, types of retained fibers in lung tissue, and diagnostic data are listed in Table 1. All cases were men, age 44 to 69 years at the diagnosis of cancer. The tissue samples were taken in 1988 to 1992 during surgical operations or at autopsies.

In one of the sprayers the size and concentration of crocidolite fibers were measured in the lung tissue of the upper left lobe, in visceral and parietal pleura adjacent to the parenchymal sampling site, in hilar lymph nodes and in the cortical tissue

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Table 1. Age, occupational history, diagnosis and parenchymal asbestos fiber concentrations in 10 workers exposed to asbestos.

Age, years	Occupation	Duration, time of exposure	Diagnosis in 1988–1992	Asbestos fibers in the lungs, $\times 10^6$ f/g	Main fiber type
47	Asbestos sprayer	20 months, 1966–68	Lung cancer, asbestosis	190	Crocidolite
49	Asbestos sprayer	8 years, 1963–71	Peritoneal mesothelioma	2700	Crocidolite
44	Asbestos sprayer	7 years, 1965–71	Peritoneal mesothelioma	3000	Crocidolite
65	Asbestos product manufacturer	3 months, 1949	Lung cancer	6	Anthophyllite
69	Asbestos product manufacturer	6 months, 1946	Lung cancer	39	Anthophyllite
58	Insulator	1 year, 1954–55	Lung cancer	13	Anthophyllite
63	Insulator	23 years, 1950–73	Lung cancer, asbestosis	65	Anthophyllite
60	Insulator	28 years, 1942–79	Pleural mesothelioma	130	Anthophyllite
63	Insulator	27 years, 1949–76	Lung cancer, asbestosis	150	Anthophyllite
55	Insulator	32 years, 1954–86	Lung cancer, asbestosis	280	Anthophyllite

of the kidneys. For comparison, asbestos fibers were also counted from lung parenchyma, lymph nodes, and kidney cortex in ten autopsied cases, collected from an unselected series of sudden Finnish male deaths.

All tissue specimens were analyzed by scanning electron microscopy (SEM) with the methods described elsewhere (*12*). Drying at 80°C, low-temperature ashing and gold coating were used for the sample preparation. Asbestos fibers >1 μm in length and >0.3 μm in diameter were identified, sized and counted at a magnification of × 5000. In the exposed cases at least 20 fibers per sample were quantified but in the reference series fewer or none were detected in the counting. The detection limit was about 0.1×10^6 fibers/g of dry tissue (f/g).

Results

The parenchymal levels were 190 to 3000 $\times 10^6$ f/g in crocidolite sprayers, 6 to 39 $\times 10^6$ f/g in asbestos product workers, and 13 to 280 $\times 10^6$ f/g in insulators (Table 1). When the exposure times and retention data were compared, the following approximative relationships were established: About 1 to 2 days of crocidolite spraying equalled to 10^6 f/g measured several years after the cessation of exposure. The corresponding index for the mixers of raw materials at the production plant was 3 to 10 days and for pipe insulators 1 to 4 months. Both groups were exposed mostly to anthophyllite. In all cases approximately 1% of the total fibers were coated asbestos bodies.

The number and size of crocidolite fibers in various tissues of one asbestos sprayer are shown in Table 2. The fiber level was highest in hilar lymph nodes, followed by lung parenchyma, visceral pleura, and parietal pleura. The concentration in the kidney cortex was 30×10^6 f/g, orders of magnitude greater than the levels found in the 10 unselected autopsies, which were in the range $<0.03–0.07 \times 10^6$ f/g with a mean value of 0.03×10^6 f/g. In this series the parenchymal levels in the range $<0.1–1.6 \times 10^6$ f/g, with a mean value of 0.5×10^6 f/g, were at or below 10^6 f/g, which is the practical limit used by our laboratory to distinguish those persons occupationally exposed to asbestos. In spite of low exposure, the concentration in the lymph nodes of the controls was in the range $5–81 \times 10^6$ f/g with a mean value of 21×10^6 f/g, which was about 40-fold higher than in the parenchyma. This was close to the ratio lymph node: parenchyma—7400×10^6:190×10^6—found in the exposed sprayer.

Table 2. Concentration and size of crocidolite fibers found in various tissues of an asbestos sprayer.

Tissue	Concentration, $\times 10^6$ f/g	Fiber length, μm		Fiber diameter, μm		Aspect ratio	
		Median	Range	Median	Range	Median	Range
Lung parenchyma	190	3.0	1–15	0.13	0.05–0.55	24	9–95
Visceral pleura	145	2.0	1–5.5	0.12	0.07–0.31	18	5–52
Parietal pleura	12	2.7	1–7.1	0.12	0.07–0.18	22	9–53
Hilar lymph node	7400	2.2	1–6.0	0.13	0.05–0.30	17	6–73
Kidney cortex	30	2.6	1–10	0.12	0.05–0.21	22	13–68

The median dimensions of crocidolite fibers were 2.0 to 3.0 μm for length, 0.12 to 0.13 μm for diameter and 17 to 24 for aspect ratio (Table 2), with no obvious difference between various tissues. Anthophyllite fibers (39×10^6 f/g) detected in the lungs of the asbestos product worker were somewhat thicker (median diameter 0.35 μm) and longer (median length 5.4 μm). The fiber dimensions of the two cases were similar to those of crocidolite and anthophyllite fibers found in larger series of mesothelioma and lung cancer cases (*12–14*). The percentage of fibers >5 μm in length was 20% for crocidolite and about 50% for anthophyllite.

Discussion

In this study we measured fiber levels in the lungs of three crocidolite sprayers and two asbestos product workers. The duration and timing of exposure were obtained from personal interviews. Roughly estimated from published data, the mean inhalation rate would be 10 m^3/8-hr work shift, the alveolar deposition, 10%, and the dry weight of the human lungs, approximately 100 g (*1,15*). Dust sampling and subsequent fiber counting by phase-contrast optical microscopy have indicated typical airborne levels of approximately 50 fibers/cm^3 > 5 μm in length in both the sprayers and the product workers. The above estimated data are consistent with a clearance half-time of 10 years or more, as calculated from a first-order kinetic model.

The cumulative equation, which gives the number of retained fibers in the lungs as number of deposited fibers minus the number of fibers cleared after exposure, depends on many parameters that are subject to considerable and unquantifiable uncertainty. Although the original levels were not known, no clearance of long amphibole fibers from the nonciliated alveolar region of the respiratory tract was demonstrable by kinetic calculations. Recent exposures to amphibole asbestos, therefore, could not be distinguished from earlier exposures since the fibers deposited in the lungs retain their initial level for decades as well as their chemical and physi-

cal properties, except for the formation of asbestos bodies.

Amphibole minerals must be cleared from the lungs, to some extent because they were present in high quantities in lymph nodes, parietal pleura, and kidneys of the exposed workers. Moreover, in this study the size and aspect ratio of the fibers in the extrapulmonary tissues were the same as those found in the parenchyma, indicating that the translocation processes have been rather unselective with respect to fiber dimensions.

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